

Bulk Flow Measurements and Angiography

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Flow sensitive MRI Techniques

It is difficult to discuss flow measurements in MRI without recognizing that magnetic resonance has a generality experienced in no other imaging modality. Signals arise from the magnetic moments which are totally controlled by three types of magnetic fields (the main, constant field, rapidly changing gradients in the main field, and radio frequency magnetic fields), which, in turn are totally under electronic and computer control. The effect of flow on the MR signal depends directly on the selected magnetic fields. For this reason, there is huge variability in the mechanisms that might be used for measuring flow.

It is also very difficult to cover the concepts of the use of MRI in flow measurements because there have been so many contributions to this field over the course of the last 20 years. In general, the first publication on a technique was based upon the accepted imaging methods of that period, and as technology has improved, the flow measurement methods have improved, and innovations have been discovered to improve measurement efficiency.

In the following we attempt to review the history of the development of flow measurement techniques, referring to as many of the fundamental contributions as we can find.

Brief History

The study of flow and its effects upon the MR signal began soon after the development of NMR itself, but proceeded at a very slow pace. The work most often cited in reviews as the earliest dealing with flow is that of Suryan, which was published in 1951.(1) Long before the development of MR imaging techniques, Suryan observed an increase in the signal from spins flowing in a tube into the signal detection region as the flow velocity was increased. He attributed the signal increase to the inflow of unsaturated spins into the region of excitation and detection. As early as 1959, J. R. Singer at the University of California, Berkeley, proposed and demonstrated that NMR could be used as a non-invasive tool to measure in vivo blood flow. (2) After earlier work by Singer with in vivo studies in mouse tails, the first human in vivo study was demonstrated by Morse and Singer.(3) This study was a rudimentary time-of-flight (TOF) effect, flipping the magnetization in the blood with a 180-degree pulse from a transmitter coil placed upstream of the receiver. In a later study, Grover and Singer exploited the effect of flow upon the phase of signal from the moving spins to extract velocity distributions.(4)

Hann demonstrated the dependence of the NMR precession phase angle on flow in the direction of a magnetic field gradient. (5) The phase effect of flow upon the signal was earlier derived by Stejskal in his work on diffusion and flow.(6)

After Singer published several experiments demonstrating that flow could be measured by signal changes in nuclear magnetic resonance, NMR flow meters were developed based upon the principles of the velocity dependence of signal washout.(7-9)

Very shortly after Paul Lauterbur and then Peter Mansfield published their papers demonstrating that Magnetic field gradients could be used in their MR imaging techniques,(10,11) Garroway was able to use magnetic field gradients to demonstrate spatial distributions of velocity profiles.(12)

In the years that followed these early pioneering studies, studies of blood vessel imaging and flow measurement techniques have grown steadily as indicated by the graph in Figure 1. Again because of the huge number of contributors and contributions, it is difficult to always determine which were the primary publications to aid in the maturing of this field.

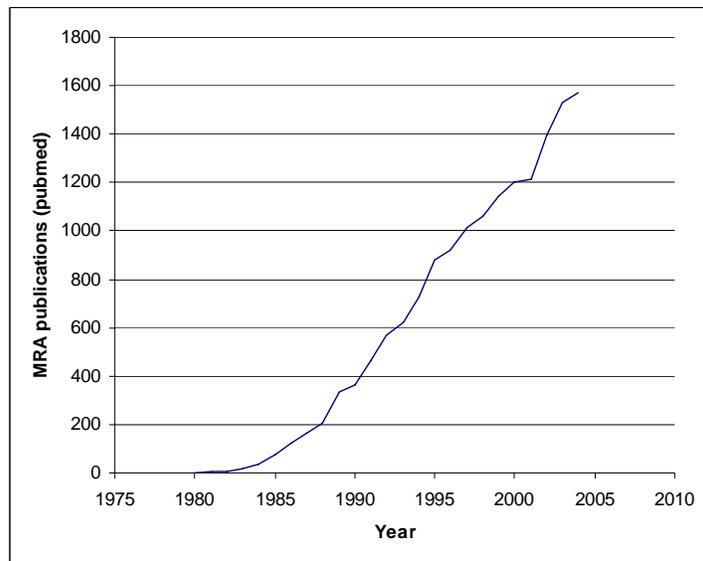


Figure 1: MRA publications from Pubmed

MRA has been important in both the imaging of blood vessels and in the determination of blood flow.

The signal in MRI arises from magnetic moments that are rotating in the transverse plane.

At the risk of oversimplification, we divide the flow imaging and measurement techniques into those in which flow changes the amplitude and those that change the phase of the rotating transverse magnetization. Because the amplitude techniques general rely on the time required for the magnetization to flow into the region being imaged, they are referred to as time-of-flight (TOF) techniques. Phase techniques can and have been used for both vessel visualization and quantitative flow measurement. In general, the inflow and saturation methods with and without injection of a T1 shortening contrast agent, have been most successful in 3D imaging of vessel anatomy while the phase techniques have been most successful for quantitative flow measurement.

Amplitude Techniques – Time-of-Flight (TOF)

The amplitude techniques can be further subdivided into a variety of methods. We will first discuss those in which the distance that the magnetization has moved is evident from the images. We will then discuss those in which the amplitude of the signal depends on velocity and the imaging technique factors.

Movement techniques.

Movement techniques are those where the magnetization is tagged in some way and then flows to give a signal that is unique and detected to be different than the signal of stationary spins.

Several different groups have studied techniques to image the distance that blood moves. In the simplest form, the magnetization within a narrow slab is saturated and after a small time interval, a slice through (perpendicular to) the slab is imaged. Any signal generated from within the saturated band is then due to blood motion and the velocity of blood can be measured by the distance of the motion.(13-15)

A similar technique designed to measure blood flow across the lumen of a vessel was developed by Saloner et al. in which the magnetization entering the region is rapidly tagged by excitations in alternate directions.(16,17) This technique produces a steady-state spatial distribution of magnetization, and hence a signal, which reflects both the time at which magnetization enters the selected slice and how long the magnetization remains in the slice. In this way, a single image can be used to extract information on the velocities of interest.

In general these "bolus tracking" techniques provide a simple method to obtain quantitative measurements of blood flow in localized regions.(18)

Adiabatic fast passage has been used to tag spins external to the imaged volume, allowing direct assessment of in-plane and oblique directional flow velocities, and visualization of flow velocity profiles.(19,20)

Amplitude effects:

The time of flight approach to imaging of flow involves the labeling of flowing magnetization prior to its entry into the imaging region of interest (ROI). The labeled volume of flowing magnetization can be referred to as a bolus. The labeling of the flowing magnetization can be done with or without RF excitation of the magnetization external to the imaging region (ROI) and a corresponding excitation within the ROI. The RF excitations and image acquisitions may be carefully timed to provide average velocity information as in Morse and Singer's one dimensional flow experiment.(3)

Prior to image acquisition, the magnetization within the imaged region can be saturated by a localized RF excitation. During the subsequent image acquisition, regions of flow bringing unsaturated magnetization into the region will appear bright in the image. Conversely, saturation RF excitations of the magnetization outside of the imaged region can make the flow appear dark in the image. Thus there are bright or "white-blood" techniques and dark or "black-blood" techniques.

In spin echo sequences, for flow through a slice, motion of the blood may cause some of the blood to not experience both the excitation (90°) and refocusing (180°) RF pulses. The signal intensity of flowing blood decreases linearly with velocity allowing quantitative measurements of high flow rates.(21)

Singer and Crooks describe a white-blood technique in a paper on blood flow measurements in the human brain.(22) Here the stationary magnetization within a

selected slice is depolarized by a 90-degree RF excitation followed by the application of strong gradients. Another 90-degree RF excitation is applied at a later time to tip the magnetization that entered the slice due to flow. Imaging is then performed using a spin echo acquisition. The timing of the 2nd 90-degree pulse and the resulting image pixel magnitude provides a measure of flow velocity. Flow rates can then be derived using the velocity measurement and vessel areas extracted from the image.

As magnetic homogeneity improved to the point that gradient recalled imaging could be performed, this method was refined to be much faster by using gradient recalled imaging instead of spin echo techniques. Again, flow through the slice of a spin-echo technique causes variations in the intensity. These variations in intensity can be directly related to the flow velocity, and allow determination of flow velocities through the slice.(23)

Hennig demonstrated that flow velocities could be measured by varying inflow times into a slice that is experiencing simultaneous steady state saturation.(24), Inflow enhancement. (25)

The use of stimulated echoes to create projection excited flow profiles that can be imaged with projection techniques, providing angiogram-like images where the extent of motion measures flow velocity.(26)

Phase Techniques

Again at the risk of oversimplification, we divide phase techniques into Fourier encoding where the full velocity distribution within a voxel is measured and phase contrast techniques where a single (average) velocity is measured.

Full Fourier encoding of flow and position.

Depending on the spatial resolution and the geometry of the flowing fluid, there may be a spectrum of velocities within the volume of a single image volume element (voxel). Paul R. Moran published one of the first papers describing the use of stepped bipolar gradient pulses to phase encode flow velocities).(27) The bipolar pulses cause a phase shift which is directly proportional to the flow velocity. By stepping the bipolar pulses and then applying a Fourier transformation, the spectrum of velocities in the direction of the bipolar gradient is obtained. Moran demonstrated that in principle it is possible to general the density of magnetic moments as a function of the 6 dimensional space of position and velocity. Although such imaging can be prohibitively long, simplifications are possible and flow distribution measurements were demonstrated by Moran et al.(28)

One such simplification was proposed by Feinberg et al. in a spin echo technique where a slice selective gradient is used to localize spins in the “z” direction, a readout gradient is used to obtain position in the “x” direction, and bipolar velocity phase encoding is used to obtain the velocity spectrum in the “y” direction (in fact this could have been any selected direction).(29) In this manner projections of the flow density function in the “y” direction are obtained. This paper also demonstrated that a 2nd spin echo could be acquired where the flow phase encoding for the first direction is “rewound” and flow phase encoding is applied in a 2nd “z” direction. Later, Feinberg and Mark(30) applied this spin echo velocity spectroscopy technique, with velocity resolution of 0.4 mm/s to measure the very low velocity distributions of CSF and the small motions of the brain. They achieved localization along a line (shaft) by applying inner volume excitation(31) where the excitation slice selection gradient along the “y” direction, the 180° slice

selection along the “z” direction and readout in the “x” direction. Velocity encoding was then applied in the expected flow direction. This technique was also used to measure flow distributions in tissue, providing information relative to tissue perfusion.(32) A similar technique using cylindrical excitation was presented by Dumoulin et al.(33)

This projection flow spectroscopy technique was improved by Hennig et al. by incorporating techniques to suppress the signal from stationary spins.(34,35) They also demonstrated that the spatial locations of the flowing signals in the projection direction could be determined by reference to blood vessel positions in conventional bright blood “FLASH” (fast low-angle shot) or rapid gradient refocused techniques.

With the development of thin slab angiography techniques,(36) Ping Hou et al. demonstrated a double echo spoiled gradient echo technique where the slice encoding gradient for the first echo image is unwound for the 2nd echo image. (37) The result is Fourier velocity encoding for that thin slab. . This technique was used to measure flow distributions in dialyzers.(38)

In order to improve the efficiency of Fourier flow methods, Dumoulin et al. introduced a technique that uses a comb excitation RF pulse to simultaneously acquire Fourier velocity encoded data from multiple slices.(39) As the Fourier velocity phase encoding gradient pulse is advanced, the phase of each slice in the comb is advanced by a unique amount, causing the signals from the magnetization in a particular slice to appear at a position in the phase encoding direction, which is the sum of the spin velocity and an offset arising from the phase increment given to that excitation slice. Velocity information is acquired simultaneously for all slices.

In general Fourier velocity techniques are very slow. In order to reduce the required acquisition time, Bittouin et al. demonstrated that the precision in flow measurements could be retained when only a few Fourier velocity encodings were performed.(40) Zero filled interpolation was used to regain fine velocity steps. Using tripolar gradient lobes, Tasu et al. were able to demonstrate Fourier acceleration images.(41)

Phase Difference due to flow

The reduced Fourier velocity encoding technique of Bittouin described just above, works well if there is only a narrow distribution of flow velocities within any single voxel. When the flow velocity is relatively constant throughout an image voxel, the result of the Fourier transform in Fourier velocity imaging techniques is a spike or delta function at the specific velocity. In this case, a single measurement of velocity dependent phase might be sufficient to determine the flow velocity. Wedeen et al. demonstrated that images obtained using conventional MRI pulse sequences often contain substantial amounts of velocity dependent phase information.(42)

One of the earliest techniques for flow measurement based upon velocity dependent phase encoding was presented by Bryant et al. (43) In this technique, two flow encoding gradient pulses in the direction perpendicular to the imaged slice, separated by a non-selective 180° RF pulse were used to encode velocity in the phase of the resulting image. In a similar technique it was shown possible to measure velocities as small as 10 μ /s.(44)

These early techniques for velocity measurement based upon bipolar flow encoding gradients were based upon the assumption that the resulting phase was only due to the velocity. Unfortunately, image phase is also affected by a variety of other factors including pulse sequence timing, B_0 (static field) inhomogeneity, B_1 (excitation RF field) phase effects, magnetic field eddy currents, and other types of motions.(45) The effects of background phase errors can be eliminated by using two different bipolar gradients and measuring the difference in the phase between the two measurements. In addition to the Fourier velocity imaging techniques which are natural examples of multiple bipolar gradients,(27,29) techniques based upon phase differences between two gradient pairs have been presented.(46-49) It was found that if the differences in the phase encodings are small, very high velocities can be recorded.(50)

If 2 bipolar pairs are necessary to encode a single velocity component, then 6 measurements could be required for measurement of the full 3 directions of flow. Hausman et al. (51) demonstrated that 3D directions of velocity components can be obtained with 4 measurements, consisting of 3 directions of velocity encoding and one zero. The early strategies for doing 3 direction flow velocity measurements are reviewed by Pelc et al. and a balanced 4 point method is presented that gives the lowest velocity variance per unit time and is more efficient than the corresponding 6 point method.(45)

Firmin et al. and Guilfoyle et al. both demonstrated that phase contrast flow encoding could be applied in single shot echo planar imaging (EPI) techniques to obtain very rapid flow velocity measurements.(52,53)

Reviews of the issues of accuracy in phase contrast and the other flow measurement techniques have been made.(54,55) In general phase contrast techniques provide a reasonable estimate of average flow velocity for unidirectional flow. Substantial errors can occur for bi-directional flow distributions.(56)

Finally, Dumoulin et al. presented a clever technique that used Fourier flow encoding for one motion component and phase contrast for a 2nd.(57) The second could be a different flow direction or acceleration.

Sources of Image artifacts and methods for artifact reduction.

Turbulent flow effects – signal loss due to intravoxel velocity dispersion. Non-constant, disordered, and turbulent flows can cause signal loss(58) which can in turn be related to the nature of the flow.(59,60)

Oblique flow artifacts – caused by the timing differences between phase encoding/velocity encoding and signal readout.(61) This artifact can be corrected by gradient moment nulling.(62) Xiang and Nalcioglu demonstrated that motion dependent pixel shifts could be used to measure flow. (63)

Image noise is always a problem, and different techniques can be used to attempt to reduce this noise on the phase velocity measurements. One in particular is spatial regularization which imposes a spatial similarity constraint on the resulting phase images.(64)

Sources of error in phase contrast measurements

There are many potential error sources and solutions. Potential errors include errors due to velocity aliasing, partial volume effects, signal loss, and image distortions due to the phase/frequency artifact.

Partial volume effects, where voxels contain both flowing fluid and stationary tissue.(65,66)

Velocity aliasing which occurs if the bipolar gradients are too large. Because velocity signal to noise ratio is inversely related to the velocity encoding gradient strength, it is advantageous to use the lowest possible encoding velocity. To avoid aliasing, 3 encoding velocities can be used. (67,68)

Signal loss due to long echo times, and pulsatile motion may be reduced by the incorporation of 3D radial trajectories, such as the cine phase contrast VIPR technique of Madison.(69)

Methods of image segmentation for flow measurement.

Quantitative flow requires integration of measurements over the dimensions of blood vessels. Segmentation of the vascular boundary can help to minimize flow errors.(70)

Potential applications of quantitative flow measurements.

There are many applications of flow measurements. The following are just minuscule example of the hundreds of published papers. Hundreds of clinical examples can be found in the literature, such as CSF flow measurements from velocity dependent phase images to name just one. (71) Of special note is the potential for making measurements that relate to vascular disease.

In measurements made of velocity profiles across the aorta above and below the renal arteries, Oshinski et al. were able to observe a lower wall shear stress in the infrarenal areas where atherosclerosis is likely to form, supporting the hypothesis that low WSS is a localizing factor for atherosclerosis, and high WSS may act as a deterrent against formation of atherosclerosis.(72)

Phase contrast velocity measurements combined with an analysis of pulse propagation has been used to estimate vascular compliance(73-77) and to estimate pressure gradients from acceleration measurements.(78)

Summary

This represents an attempt to review the techniques that have been and might be used in the quantitative measurement of fluid flow. In so doing we have reviewed the history of the measurements. In fact, this history has been based upon the innovation of many bright and capable researchers operating with the constraints of the slowly evolving MRI technology. Currently amplitude techniques are primarily used (without and with Gd. contrast agents) in the visualization of blood vessel anatomy. Phase contrast techniques are used for velocity and flow measurements. But the techniques continue to evolve rapidly and progress in flow, motion, and related measurement techniques can be expected to evolve extensively during the foreseeable future.

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